

## **REMARKS**

Reconsideration and withdrawal of the rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks, which place the application in condition for allowance.

### **I. STATUS OF CLAIMS AND FORMAL MATTERS**

Claims 22-49 are pending. Claims 1-15 and 17-21 are cancelled and new claims 22-49 added without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are patentably distinct from the references cited by the Examiner, and that these claims are in full compliance with the requirements of 35 U.S.C. §112. The addition of the claims herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

Support for the new claims is found throughout the specification and from the cancelled claims.

### **II. THE REJECTION UNDER §112, FIRST PARAGRAPH, IS OVERCOME**

Claims 1-7, 9-15 and 17-21 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing non-enabling subject matter. The Office Action contends that only limited forms of formula (I) have been shown to be effective for the claimed control, but not for all compounds or compound groups. Applicants disagree.

Applicants' invention is clearly enabled because a skilled artisan would readily understand that the claimed compounds must have the ability to eradicate fleas in domestic or accommodation premises. Further, the Examiner is directed to pages 11-13 of the application which discuss the efficacy of combining other parasiticides with the compounds of formula (I) or (II). Predictability in the art did exist at the time of filing and, coupled with the knowledge of a skilled artisan and the guidance of the present application, there is sufficient evidence that Applicants' disclosure does satisfy the enablement requirement.

Furthermore, phenylpyrazoles are a class of insecticides which possess excellent insecticidal activity against insect pests including blood-sucking pests such as ticks, and fleas etc., which are parasites on animals. Phenylpyrazoles are within the class of compounds known as arylheterocycles. This class of agents kills insects by acting on the gamma-butyric acid (GABA) receptor of invertebrates (*See, e.g.,* Bloomquist, Ann Rev Entomol, 41:163-90 (1996) (Abstract attached)).

The compounds according to formula (I) are very lipophilic and of high vapor pressure (low volatility). Thus, the compounds have a very high affinity for the sebum and are taken up by the sebaceous glands. Indeed, Cochet et al., Eur J Drug Metab Pharmacokinet 22(3):211-6 (1997) (copy of Abstract attached) showed that fipronil, an exemplary compound within formula (I), indeed is taken up in the sebaceous glands (and epithelial layers) of animals. Since the compounds of formula (I) are very lipophilic and of high vapor pressure (low volatility) there is no reason to doubt that they too, like fipronil, will be taken up in the sebaceous glands (and epithelial layers) of animals.

Hainzl et al., PNAS USA 93(23):1276407 (1996) (copy of Abstract attached) showed that desulfinylfipronil, the trifluoromethylpyrazole derivative of fipronil, is formed when fipronil is used as a plant insecticide (exposed to sunlight). Hainzl et al. 1996 also showed that desulfinylfipronil, the trifluoromethylpyrazole derivative of fipronil, a phenylpyrazole related to fipronil, has high neuroactivity, like fipronil and suggests that desulfinylfipronil can be a significant contributor to the effectiveness of fipronil as an insecticide for crop protection.

Since fipronil derivatives have neurotoxicity, there is no reason to doubt that compounds of formula (I) will likewise be active against fleas and ticks. Hainzl et al. 1996 states that the trifluoromethylsulfinyl moiety of fipronil is "presumably important in its outstanding performance." In this regard, note that in formula (I) compounds, it is preferred that  $R_2$  be  $S(O)_nR_3$  with  $R_3$  being preferably ethyl or haloalkyl (application at page 4), with particular mention being made of formula (I) compounds wherein  $n=0$  and  $R_3$  is  $CF_3$ , and formula (I) compounds wherein  $n=1$  and  $R_3$  is ethyl (application at page 4). Further page 5 teaches a preferred class of compounds of formula (I) consists of those wherein  $R_1$  is CN,  $R_3$  is haloalkyl,  $R_4$  is  $NH_2$ ,  $R_{11}$  and  $R_{12}$  are, independently of each other, is a halogen atom, and/or  $R_{13}$  is haloalkyl.

Thus the skilled artisan, looking to the specification, is directed to compounds of formula (I) having the trifluoromethylsulfinyl moiety of fipronil which is recognized as "important in its outstanding performance", as well as to formula (I) compounds wherein  $n=0$  and  $R_3$  is  $CF_3$  or wherein  $n=1$  and  $R_3$  is ethyl (and thus  $R_2$  is  $S(O)_nR_3$ ), and compounds of formula (I) wherein  $R_1$  is CN,  $R_3$  is haloalkyl,  $R_4$  is  $NH_2$ ,  $R_{11}$  and  $R_{12}$  are, independently of each other, is a halogen atom, and  $R_{13}$  is haloalkyl (and thus  $R_2$  is  $S(O)_nR_3$ ), such that the specification provides a great deal of guidance, in addition to the Examples as to compounds within formula (I) that are especially useful in the practice of the invention; and, the skilled artisan would likely initially select those preferred compounds in any screening.

Further still, Hainzl et al. 1996 was followed by Hainzl et al., Chem Res Toxicol 11(12):1529-35 (1998) (copy of Abstract attached), wherein the authors showed that phenylpyrazoles related to fipronil, such as desulfinyl fipronil and fipronil sulfone, indeed acted on the GABA receptor of insects. Thus those compounds too will act as insecticides, like fipronil.

Accordingly, it is clear that compounds in addition to fipronil, within formula (I), act as insecticides; and, there is no reason to doubt that a sufficient number of compounds within formula (I) function to kill fleas and ticks. Also, it is clear that the specification provides guidance as to compounds within formula (I) which should perform like fipronil (especially considering literature such as Hainzl et al. 1996 and Hainzl et al. 1998).

In addition, given that the insecticide mode of action of fipronil and of phenylpyrazoles within formula (I) is known (namely acting on the GABA receptor by blocking the chloride channel), no undue experimentation is required to test the insecticidal action of any compound within formula (I): One need only test compounds for this mode of action, or neuroactivity (or neurotoxicity), or for  $IC_{50}$ ; e.g., as in Hainzl et al. 1996 and Hainzl et al. 1998.

Thus, it is respectfully submitted that the assertion in the Office Action that the claims are not enabled is obviated.

Consequently, the Section 112, first paragraph, rejection should be reconsidered and withdrawn; and, such relief is respectfully requested.

**III. THE REJECTIONS UNDER §112, SECOND PARAGRAPH, ARE OVERCOME**

Claims 1-15 and 17-21 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. The cancellation of claims 1-15 and 17-21, and the addition of new claims 22-49, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, have rendered the Section 112, second paragraph, rejections moot.

Consequently, reconsideration and withdrawal of the objection is believed to be in order and such action is respectfully requested.

**IV. THE REJECTIONS UNDER §102 ARE OVERCOME**

Claims 1-14 and 18-20 stand rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 6,096,329 to Jeannin et al. ("329 patent"). This rejection is respectfully traversed.

It is respectfully pointed out that the '329 patent is not a proper 102(e) reference. The '329 patent has inventors that overlap with the present inventors. Therefore, the '329 patent does not represent the work of "another" as required by Section 102(e). In this regard, attention is respectfully invited to *In re Kaplan*, 789 F.2d 1574, 229 U.S.P.Q. 678 (Fed. Cir. 1986) and *Applied Materials v. Gemini Research Corp.*, 5 U.S.P.Q.2d 1127, 1129-30 (Fed. Cir. 1988), wherein the Federal Circuit held that "though an application and a patent have ... different inventive entities, if they share one or more persons as joint inventors, the 35 U.S.C. §102(e) exclusion for a patent granted to 'another' is not necessarily satisfied."

If called upon, Applicants will provide a Declaration under 37 C.F.R. 1.132 pursuant to M.P.E.P. §706.02 further demonstrating that the inventive entity in the '329 patent is not "another" as to the inventive entity of the present application under 35 U.S.C. §102(e); but, in view of the case law discussed herein, such is not believed necessary.

Consequently, the rejection is obviated. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-12 and 17-21 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Frontline brochure ("Frontline") or MEO et al., *Proc. Am. Assoc. Vet. Parasitol.* (41 Meet., 52, 1996) ("MEO"). Claims 1, 9-15 and 18-20 stand rejected under 35 U.S.C. §102(b) as allegedly

anticipated by Sirinyan, DE 4443888 ("DE '888"). And, claims 1-12 and 18-20 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Mizutani et al., WO 9616544 ("WO '544"). These rejections will be addressed collectively and are respectfully traversed. None of the cited references anticipate the instant invention.

Applicants' invention is directed to, *inter alia*, a method for the eradication of fleas in domestic or accommodation premises of a domestic or laboratory mammal, comprising topically applying, at least monthly to a localized region having a surface area between 5 and 10 cm<sup>2</sup> on the domestic or laboratory mammal, a parasitically effective amount of a spot-on topical preparation comprising a veterinarily acceptable vehicle and a compound of Formula I or Formula II, wherein the preparation is so applied to the mammal, through the action of the compound and the vehicle, that the compound diffuses over the mammal's body, and then dries without crystallization and without modifying the mammal's appearance and coat.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. See *Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. See *Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. See *In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, the references relied upon by the Office Action do not disclose, suggest or enable Applicants' invention. Firstly, none of the references contain all of the elements of the instant claims. Claim 22, support for which is from cancelled claim 1 and presented to better clarify the scope of Applicants' invention, provides for a method of, *inter alia*, eradicating fleas in domestic or accommodation premises by applying a parasitically effective amount of a spot-on topical preparation comprising a veterinarily acceptable vehicle and a compound of Formula I or Formula II. None of the cited references read on the instant claims. Secondly, none of the cited references enable Applicants' invention, which provides for a method of, *inter alia*, eradicating fleas in domestic or accommodation premises by applying a parasitically effective amount of a spot-on topical preparation comprising a veterinarily

acceptable vehicle and a compound of Formula I or Formula II. For these reasons alone, the Section 102 rejections should be obviated.

Consequently, reconsideration and withdrawal of the Section 102 rejections are believed to be in order and such action is respectfully requested.

**V. THE REJECTIONS UNDER §103 ARE OVERCOME**

Claims 1-15 and 17-21 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over the Frontline Brochure ("Frontline) or Mizutani et al., WO 9616544 ("WO '544"), in view of EP 05165590 to Chatfield et al. ("EP '590"), MEO et al., *Proc. Am. Assoc. Vet. Parasitol.* (41 Meet., 52, 1996) ("MEO"), and Sirinyan et al., DE 4443888 ("DE '888"). The rejections are traversed as none of the cited references teach, suggest or motivate one skilled in the art to achieve the present invention.

As explained above, Applicants' invention is directed to, *inter alia*, a method for eradicating fleas in domestic or accommodation premises of a domestic or laboratory mammal, comprising topically applying, at least monthly to a localized region having a surface area between 5 and 10 cm<sup>2</sup> on the domestic or laboratory mammal, a parasitically effective amount of a spot-on topical preparation comprising a veterinarily acceptable vehicle and a compound of Formula I or Formula II. None of the cited references disclose such a method, nor suggest or motivate a skilled artisan to practice such a method.

Frontline relates to the treatment of a pet with Frontline spray, i.e., spraying the formulation over the animal. WO '544 relates to the use of an emulsifiable composition containing a phenyl pyrazole. EP' 590 relates to a method of controlling or eliminating pest-infestation of domestic animals which employs the animals as vectors for pest control agents. MEO relates to the treatment of a pet by spraying Frontline over the animal. Finally, DE '888 relates to use of imidacloprid and possible combination with other parasiticides such as IGRs

The Examiner is respectfully reminded of the case law; namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine*, 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere

fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification.” Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

One of the unique features of Applicants' invention is that fleas are eradicated from domestic or accommodation premises by applying the instant formulation as a spot-on onto the domestic or laboratory mammal. All the cited references are distinguishable from Applicants' invention. To wit, and taking the references slightly out of turn, Frontline and MEO do not disclose treatment of the premises upon spot-on treatment of the animal. Indeed, both references involve spraying of the animal, and nowhere is spot-on disclosed, taught, suggested or implied. Thus, the rejections based on these references are obviated.

DE '888 is even more deficient. DE '888 relates to use of imidacloprid, in possible combination with other parasitocides such as IGRs. Example 1 of DE '888 relates to a dermal formulation on dogs. Daily treatment is suggested, but it is believed that periodical infestation with fleas was conducted by putting the fleas directly onto the animal (*see* page 15, lines 45-46). Moreover, there is no indication in DE '888 whether the animals were kept in any specific premises. Indeed, there is no suggestion that the treatment of the dogs also eradicated fleas in the premises. Therefore, the rejection based on DE '888 is obviated.

Similarly, with respect to WO '544, there is no indication of a treatment of the premises of the animal, nor any suggestion or disclosure of an effect on the premises. Instead, WO '544 relates to a method of controlling termites wherein the composition is applied to the infested locus. There is no teaching or suggestion in WO '544 that would lead a skilled artisan to practice a method of controlling fleas in the premises of pets. The rejection based on WO '544 is, therefore, obviated.

Finally, EP '590 does not suggest or motivate one skilled in the art to use fipronil or pyrazoles to treat the premises. EP '590 relates to the animal acting as a vector to spread substantial amounts of insecticide onto the surface of the premises. Such a transfer of a substantial amount of insecticide is a serious drawback and is surprisingly avoided in the present invention, wherein the instant formulation, such as fipronil or other pyrazoles, remain substantially on the animal. In fact, one way that the instant invention achieves flea eradication

is not by direct contact of the insecticide with the insect or parasite in the premises, but by a control during the part of the life cycle of the parasite where the parasite remains on the animal. Indeed, this control is due to the fact that the parasitocides of the instant invention are so efficient on the animal that the life cycle of the fleas is interrupted on the animal such that the fleas and flea eggs are no longer present in the premises. This unexpected result obviates the need, as disclosed in EP '590, to use the animal as a vector to spread the parasiticide directly onto the premises. Therefore, as EP '590 does not suggest or motivate a skilled artisan to use a spot-on formulation to eradicate fleas in the premises, and since the instant invention achieves, *inter alia*, unexpected results along the foregoing lines, the rejection based on EP '590 is obviated.

Further, it cannot be argued that any of the references inherently achieve flea eradication of the premises. It is not enough for one to contend that the compounds or methods in the relied-upon references "inherently" speak to the instantly claimed invention. The references must disclose or suggest the properties for inherency to attach. According to *In re Rijckaert*, 9 F.3d 1531, 1957 (Fed. Cir. 1993), "such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection." The Federal Circuit is clear that "inherency...may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency]." *Continental Can Company v. Monsanto Company*, 948 F.2d 1264, 1269 (Fed. Cir. 1991), citing to *In re Oelrich*, 666 F.2d 578, 581-582 (C.C.P.A. 1981). Indeed, "before a reference can be found to disclose a feature by virtue of its inherency, one of ordinary skill in the art viewing the reference must understand that the unmentioned feature at issue is *necessarily* present in the reference." *SGS-Thomson Microelectronics, Inc. v. International Rectifier Corporation*, 31 F.3d 1177 (Fed. Cir. 1994) (emphasis in original). Applying the law to the instant facts, none of the references cited in the Office Action inherently teach, disclose or suggest Applicants' invention. That is, none of the references inherently teach, disclose or suggest eradication of fleas in domestic or accommodation premises by the spot-on application of the instant formulations on the mammal. Thus, inherency cannot attach.

Consequently, reconsideration and withdrawal of the rejections are believed to be in order and such action is respectfully requested.



**VI. RESPONSE TO RESTRICTION REQUIREMENT**

The October 12, 2000 Office Action required an election under 35 U.S.C. § 121 from:

**Group I.** Claims 1-15 and 18-20, drawn to methods, classified in class 424, subclass 405.

**Group II.** Claims 17 and 21, drawn to kits, classified in class 206, subclass 528.

Applicants provisionally elect, with traverse, for further prosecution in this application, the invention of Group I, claims 11-19, now claims 22-49, drawn to methods, classified in class 424, subclass 405. Further, Applicants provisionally elect, with traverse, fipronil.

Reconsideration and withdrawal of the restriction requirement are respectfully requested in view of the remarks herewith.

The present invention relates to a procedure for the eradication of parasites, namely parasites of the order of *Siphonaptera*, especially fleas, such as, for example, *Ctenocephalides felis* and *canis*, but likewise the other fleas of small mammals such as, for example, rabbits or laboratory animals. The present invention also relates to a procedure for the eradication of fleas in domestic and accommodation premises of mammals of small size, especially cats and dogs, characterized in that a concentrated topical preparation for point application, of the spot-on type in an efficaciously parasitocidal quantity of a compound of the formula (I) or, optionally, of formula (II) is applied periodically to the animal or the animals of the premises considered, according to a monthly periodicity.

The present claims, therefore, represent a web of knowledge and continuity of effort that merits examination in a single application. Indeed, the claims of Groups I and II are related since the claims of Group II comprise units of the compositions recited in the claims of Group I. Moreover, all of the claims are directed to the eradication of fleas in domestic or accommodation premises of mammals of small size using a parasitically effective amount of compounds of formula (I) or formula (II).

In this regard, the Examiner's attention is respectfully requested to review MPEP § 808.02 which states, "even with patently distinct inventions, restriction is not (emphasis added) required unless one of the following reasons appears:

1. Separate classification;

2. Separate status in the art; or
3. Different field of search[.]”

Contrary to the guideline mandated by the MPEP, Groups I and II involve eradication of fleas utilizing a parasitically effective amount of compounds of formula (I) or formula (II), thereby encompassing the same field of search. Thus, restriction is not appropriate.

Additionally, the Examiner's attention is further respectfully invited to review the text of MPEP § 803 which in part states:

If the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions (emphasis added).

Thus, the mere allegation that the two Groups identified in the Office Action are distinct ignores the chemical interrelationship. Examination of any of these groups mandates consideration of the patentable elements in all of them.

There is no showing in the Office Action that there would be any undue or serious burden in examining Groups I and II in this application. That is, there has been no showing of any undue or serious burden in searching and examining the method of killing fleas utilizing a parasitically effective amount of compounds of formula (I) or formula (II) and the kits utilizing the units of the compounds claimed therein. The link between the groups is the parasitically effective amount of the compounds of formula (I) or formula (II). Consequently, there is a concept that links the Groups and shows that search and examination should not be serious or undue. Accordingly, it is respectfully submitted that the Office Action is fatally defective and the restriction requirement cannot stand.

In summary, enforcing the present restriction requirement would result in inefficiencies and unnecessary expenditures by both the Applicants and the PTO, as well as extreme prejudice to Applicants (particularly in view of GATT, a shortened patent term may result in any divisional applications filed). Restriction has not been shown to be proper, especially since the requisite showing of serious burden has not been made in the Office Action and there are relationships between the claims both of these Groups. Indeed, the search and examination of each Group is likely to be co-extensive and, in any event, would involve such interrelated art that the search

and examination of the entire application can be made without undue burden on the Examiner.  
All of the preceding, therefore, mitigate against restriction.

**REQUEST FOR INTERVIEW**

If any issue remains as an impediment to allowance, an interview with the is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

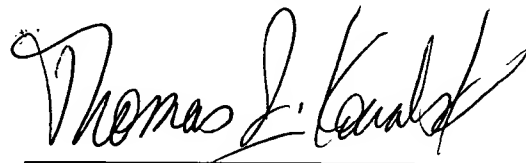
**CONCLUSION**

In view of the remarks and amendments herewith and those of record, the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance, or an interview at a very early date with a view to placing the application in condition for allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,

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